Amendments to the Specification:

Please enter into the specification the attached paper copy of the Sequence Listing which includes 6 pages and provides sequences identified as SEQ ID NO:s 1-2.

On page 1, in the paragraph on lines 9-12, the text is amended as follows:

-- This is a continuation application of application serial no. 09/322,875 filed May 28, 1999, which is a continuation-in-part application of ~~pending~~ application serial no. 09/237,299 filed January 25, 1999, which claims priority under Section 119(e) to provisional application number 60/072,481 filed January 26, 1998, now abandoned, the contents of which are incorporated herein by reference. --

On page 3, in the paragraph on lines 5-23, the text is amended as follows:

-- Induction of various cellular responses mediated by such TNF family cytokines is believed to be initiated by their binding to specific cell receptors. Two distinct TNF receptors of approximately 55-kDa (TNFR1) and 75-kDa (TNFR2) have been identified [Hohmann et al., J. Biol. Chem., 264:14927-14934 (1989); Brockhaus et al., Proc. Natl. Acad. Sci., 87:3127-3131 (1990); EP 417,563, published March 20, 1991] and human and mouse cDNAs corresponding to both receptor types have been isolated and characterized [Loetscher et al., Cell, 61:351 (1990); Schall et al., Cell, 61:361 (1990); Smith et al., Science, 248:1019-1023 (1990); Lewis et al., Proc. Natl. Acad. Sci., 88:2830-2834 (1991); Goodwin et al., Mol. Cell. Biol., 11:3020-3026 (1991)]. Extensive polymorphisms have been associated with both TNF receptor genes [see, e.g., Takao et al., Immunogenetics, 37:199-203 (1993)]. Both TNFRs share the typical structure of cell surface receptors including extracellular, transmembrane and intracellular regions. The extracellular portions of both receptors are found naturally also as soluble TNF-binding proteins [Nophar, Y. et al., EMBO J., 9:3269 (1990); and Kohno, T. et al., Proc. Natl. Acad. Sci. U.S.A., 87:8331 (1990)]. More recently, the cloning of recombinant soluble TNF receptors was reported by Hale et al. [J. Cell. Biochem. Supplement 15F, 1991, p. 113 (P424)]. --

On page 3, in the paragraph on lines 38-41 - page 4, lines 1-17, the text is amended as follows:

-- A similar repetitive pattern of CRDs exists in several other cell-surface proteins, including the p75 nerve growth factor receptor (NGFR) [Johnson et al., Cell, 47:545 (1986); Radeke et al., Nature, 325:593 (1987)], the B cell antigen CD40 [Stamenkovic et al., EMBO J., 8:1403 (1989)], the T cell antigen OX40 [Mallett et al., EMBO J., 9:1063 (1990)] and the Fas antigen [Yonehara et al., supra and Itoh et al., Cell, 66:233-243 (1991)]. CRDs are also found in the soluble TNFR (sTNFR)-like T2 proteins of the Shope and myxoma poxviruses [Upton et al., Virology, 160:20-29 (1987); Smith et al., Biochem. Biophys. Res. Commun., 176:335 (1991); Upton et al., Virology, 184:370 (1991)]. Optimal alignment of these sequences indicates that the positions of the cysteine residues are well conserved. These receptors are sometimes collectively referred to as members of the TNF/NGF receptor superfamily. Recent studies on p75NGFR showed that the deletion of CRD1 [Welcher, A.A. et al., Proc. Natl. Acad. Sci. USA, 88:159-163 (1991)] or a 5-amino acid insertion in this domain [Yan, H. and Chao, M.V., J. Biol. Chem., 266:12099-12104 (1991)] had little or no effect on NGF binding [Yan, H. and Chao, M.V., supra]. p75 NGFR contains a proline-rich stretch of about 60 amino acids, between its CRD4 and transmembrane region, which is not involved in NGF binding [Peetre, C. et al., Eur. J. Hematol., 41:414-419 (1988); Seckinger, P. et al., J. Biol. Chem., 264:11966-11973 (1989); Yan, H. and Chao, M.V., supra]. A similar proline-rich region is found in TNFR2 but not in TNFR1. --

On page 6, in the paragraph on lines 3-29, the text is amended as follows:

-- As presently understood, the cell death program contains at least three important elements - activators, inhibitors, and effectors; in *C. elegans*, these elements are encoded respectively by three genes, *Ced-4*, *Ced-9* and *Ced-3* [Steller, Science, 267:1445 (1995); Chinnaiyan et al., Science, 275:1122-1126 (1997); ~~Wang~~ Zou et al., Cell, 90:~~1-20~~ 405-413(1997)]. Two of the TNFR family members, TNFR1 and Fas/Apo1 (CD95), can activate apoptotic cell death [Chinnaiyan and Dixit, Current Biology, 6:555-562 (1996); Fraser and Evan, Cell; 85:781-784 (1996)]. TNFR1 is also known to mediate activation of the transcription factor, NF-KB [Tartaglia et al., Cell, 74:845-853 (1993); Hsu et al., Cell, 84:299-308 (1996)]. In addition to some ECD homology, these two receptors share homology in their intracellular domain (ICD) in an

oligomerization interface known as the death domain [Tartaglia et al., supra; Nagata, Cell, 88:355 (1997)]. Death domains are also found in several metazoan proteins that regulate apoptosis, namely, the Drosophila protein, Reaper, and the mammalian proteins referred to as FADD/MORT1, TRADD, and RIP [Cleaveland and Ihle, Cell, 81:479-482 (1995)]. Upon ligand binding and receptor clustering, TNFR1 and CD95 are believed to recruit FADD into a death-inducing signaling complex. CD95 purportedly binds FADD directly, while TNFR1 binds FADD indirectly via TRADD [Chinnaiyan et al., Cell, 81:505-512 (1995); Boldin et al., J. Biol. Chem., 270:387-391 (1995); Hsu et al., supra; Chinnaiyan et al., J. Biol. Chem., 271:4961-4965 (1996)]. It has been reported that FADD serves as an adaptor protein which recruits the *Ced-3*-related protease, MACHα /FLICE (caspase 8), into the death signaling complex [Boldin et al., Cell, 85:803-815 (1996); Muzio et al., Cell, 85:817-827 (1996)]. MACHα/FLICE appears to be the trigger that sets off a cascade of apoptotic proteases, including the interleukin-1β converting enzyme (ICE) and CPP32/Yama, which may execute some critical aspects of the cell death program [Fraser and Evan, supra]. --

On page 7, in the paragraphs on lines 24-31, the text is amended as follows:

-- Figures 1A-1B shows the nucleotide sequence (SEQ ID NO:~~2~~ 1) of a cDNA for human DR4 and its derived amino acid sequence (SEQ ID NO:~~1~~ 2). The respective nucleotide and amino acid sequences for human DR4 are also reported in Pan et al., Science, 276:111 (1997).

Figures 2A-2B shows the FACS analysis of two anti-DR4 antibodies, 4E7.24.3 ("4E7") and 4H6.17.8 ("4H6") (illustrated by the bold lines) as compared to IgG controls (dotted lines). Both antibodies recognized the DR4 receptor expressed in human 9D cells. --

On page 8, in the paragraph on lines 1-3, the text is amended as follows:

-- Figures 6A-6B ~~is a~~ are graphs showing results of an ELISA testing binding of DR4 antibodies, 4E7.24.3 and 4H6.17.8, to DR4 and to other known Apo-2L receptors referred to as Apo-2, DcR1, and DcR2. --

On page 8, in the paragraph on lines 15-17, the text is amended as follows:

-- Figures 9A-9B ~~shows~~ apoptotic activity of DR4 antibodies, 4H6, 4E7, 4G7, 4G10.20.6 ("4G10"), 3G1.17.2 ("3G1"), 5G11, 1H8.17.5 ("1H8"), and 1H5.24.9 ("1H5") on SKMES colon tumor cells in the presence of goat anti-mouse IgG Fc. --

On page 9, in the paragraphs on lines 8-40 - page 10, lines 1-2, the text is amended as follows:

-- A receptor for Apo-2L has been identified and referred to as DR4, a member of the TNF-receptor family that contains a cytoplasmic "death domain" capable of engaging the cell suicide apparatus [see Pan et al., Science, 276:111 (1997)]. The term "Death Receptor 4" or "DR4" when used herein encompasses native sequence DR4 and DR4 variants (which are further defined herein). These terms encompass DR4 expressed in a variety of mammals, including humans. DR4 may be endogenously expressed as occurs naturally in a variety of human tissue lineages, or may be expressed by recombinant or synthetic methods. A "native sequence DR4" comprises a polypeptide having the same amino acid sequence as a DR4 derived from nature. Thus, a native sequence DR4 can have the amino acid sequence of naturally-occurring DR4 from any mammal. Such native sequence DR4 can be isolated from nature or can be produced by recombinant or synthetic means. The term "native sequence DR4" specifically encompasses naturally-occurring truncated or secreted forms of the DR4 (*e.g.*, a soluble form containing, for instance, an extracellular domain sequence), naturally-occurring variant forms (*e.g.*, alternatively spliced forms) and naturally-occurring allelic variants of the DR4. In one embodiment of the invention, the native sequence DR4 is a mature or full-length native sequence DR4 comprising amino acids 1 to 468 of Fig. 1 (SEQ ID NO:~~1~~ 2).

The terms "extracellular domain" or "ECD" herein refer to a form of DR4 which is essentially free of the transmembrane and cytoplasmic domains of DR4. Ordinarily, DR4 ECD will have less than 1% of such transmembrane and/or cytoplasmic domains and preferably, will have less than 0.5% of such domains. Optionally, DR4 ECD will comprise amino acid residues 1 to 218 or residues 24 to 218 of Fig. 1 (SEQ ID NO:~~1~~ 2).

"DR4 variant" means a biologically active DR4 having at least about 80% or 85% amino acid sequence identity with the DR4 having the deduced amino acid sequence shown in Fig. 1 (SEQ ID NO:~~1~~ 2) for a full-length native sequence human DR4. Such DR4 variants include, for instance, DR4 polypeptides wherein one or more amino acid residues are added, or deleted, at the N- or C-terminus

of the sequence of Fig. 1 (SEQ ID NO:~~1~~ 2). Ordinarily, an DR4 variant will have at least about 80% amino acid sequence identity, more preferably at least about 90% amino acid sequence identity, and even more preferably at least about 95% amino acid sequence identity with the amino acid sequence of Fig. 1 (SEQ ID NO:~~1~~ 2). --

On page 31, in the paragraph on lines 15-20, the text is amended as follows:

-- At the end of the incubation, cells were washed once with PBS. The washed cells were resuspended in 200 microliter binding buffer (Clontech) and 10 microliter of FITC-Annexin V (Clontech) and 10 microliter of propidium iodide were added to the cells. [See, Moore et al., Methods in Cell Biol., 57:265 (1998)]. After incubation for 15 minutes in the dark, the cells were analyzed by FACScan. --

On page 35, in the paragraph on lines 24-32, the text is amended as follows:

-- The following materials have been deposited with the American Type Culture Collection, 10801 University Boulevard, Manassas, Virginia, USA (ATCC):

Material	ATCC Dep. No.	Deposit Date
4E7.24.3	HB-12454	Jan. 13, 1998
4H6.17.8	HB-12455	Jan. 13, 1998
1H5.25.9	HB-12695	April 1, 1999
4G7.18.8	PTA- 99	May 21, 1999
5G11.17.1	HB-12694	April 1, 1999 --